

REMARKS

I. Introduction

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow. Applicants thank the Examiner for the allowance of claims 1-6.

Claims 7, 8 and 16 are currently amended. Claims 8-15 are withdrawn. Claims 1-7 and 16-21 have been examined. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claims remain under examination in the application, is presented, with an appropriate defined status identifier.

Applicants have amended claim 8 in parallel with the other claims and request rejoinder of the withdrawn claims upon allowance of the case.

Upon entry of this Amendment, claims 1-21 will remain pending in the application.

Because the foregoing amendments do not introduce new matter, entry thereof by the Examiner is respectfully requested.

II. Response to Issues Raised by Examiner in Outstanding Office Action

a. Objections to the Specification

Applicants have provided an appropriate "Brief Description of the Drawings" section as requested by the Examiner and request withdrawal of this objection. See Office Action , p. 2.

b. Claim Rejections - 35 U.S.C. § 112, second paragraph

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as indefinite. See Office Action, p. 2. Following the Examiner's suggestion, the claim was limited by the language "consisting essentially of" and is now in condition to allowance. Applicants respectfully request reconsideration and withdrawal of the rejection.

c. Claim Rejections - 35 U.S.C. § 102

Claims 16 and 17 stand rejected under 35 U.S.C. 102 (b) as anticipated by Yamashita in the light of Barka. The Office states,

...Yamashita et al teaches a culture system for culturing intestinal epithelial cells that comprises basic culture medium BCM, differentiation medium DM and butyrate (page 671, table 1 , protocol). The BCM includes DMEM supplemented with 1% NEAA and 10% FBS (page 670, col. 1, par. 3). The DM contains MITO Extender (page 671, col. 2).

Office Action, p. 3. While referring to the evidence by Barka, the Examiner states, “The MITO extender contains transferrin, insulin, epithelial growth factor (EGF), hydrocortisone, progesterone and testosterone...” Id.

However, as evidenced by Barka, the MITO extender additionally contains endothelial cell growth supplement, tri-iodothyronine, estradiol-17, selenous acid, and O-phosphorylethanolamine, which are absent from the invention as currently claimed. See Barka, p. 1454, col. 2. Therefore, Yamashita and Barka do not teach a composition consisting essentially of the enumerated components of claims 16 and 17. Since the cited references do not teach each and every element of the claimed invention, they cannot serve as the basis for an anticipation rejection.

Applicants note that the composition of the current invention is clearly advantageous to the Yamashita composition, which contains additional ingredients, in terms of 1) markedly enhanced TEER (see, for comparison, Fig. 4 of Yamashita and Fig.1, HTB-10 medium of the current application), 2) permeability values for mannitol and atenolol that are much closer to those of traditional 21-day systems, and 3) the ability to differentiate between the low (mannitol) and high (propranolol) permeability compounds (see, for comparison, Table 2 of Yamashita and Table 1 of the current invention).

Applicants respectfully request reconsideration and withdrawal of the rejection.

d. Claim Rejections - 35 U.S.C. § 103

Further, Claims 7 and 16-21 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Yamashita, Barka, and Parenteau (US 5712163 ('163)). Applicants respectfully request reconsideration and withdrawal of the rejection.

The Examiner asserts that Yamashita, as evidenced by Barka, teaches a culture system composition for culturing intestinal epithelial cells that comprises a basic cell culture medium DMEM, serum, non-essential amino acids, butyrate, transferrin, insulin, epithelial growth factor (EGF), hydrocortisone, progesterone, and testosterone. However, since these references are silent with regards the concentrations of the some supplements and hormones, the Office uses '163 to allegedly teach concentrations of transferrin, insulin, EGF, and hormones within the presently claimed ranges. Office Action, pp. 4-6.

To establish a *prima facie* case of obviousness, there needs to be (1) some suggestion or motivation to modify the reference or to combine reference teachings, (2) a reasonable expectation of success, and (3) the prior art references, when combined, must teach or suggest all the limitations of the claimed invention. See MPEP §2143 (Aug. 2001). "Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). Applicants respectfully assert that the examiner has not met his burden.

Yamashita does not teach or suggest the instant invention because Yamashita, as evidenced by Barka, requires a medium comprising the following components: transferrin, insulin, epithelial growth factor (EGF), hydrocortisone, progesterone, testosterone, endothelial cell growth supplement, tri-iodothyronine, estradiol-17, selenous acid, and O-phosphorylethanolamine, and does not teach or suggest a composition for culturing intestinal epithelial cells comprising fewer than all of these components. In contrast, the current claims recites a composition for culturing intestinal epithelial cell lines consisting essentially of cell culture growth medium supplemented with fetal bovine serum, nonessential amino acids, human transferrin, bovine insulin, human epithelial growth factor, sodium butyrate, hydrocortisone, progesterone, and testosterone. See independent claims 1, 8, and 16, as well

as currently amended claim 7. There is no teaching or suggestion in Yamashita to limit the essential components enumerated in the reference to produce a suitable medium.

Moreover, the composition of the current invention shows superior and unexpected results in comparison to Yamashita, with regards to: 1) markedly enhanced TEER (see, for comparison, Fig. 4 of Yamashita and Fig.1, HTB-10 medium of the current application), 2) permeability values for mannitol and atenolol that are much closer to those of traditional 21-day systems, and 3) the ability to differentiate between the low (mannitol) and high (propranolol) permeability compounds (see, for comparison, Table 2 of Yamashita and Table 1 of the current invention).

'163 does not remedy the deficiencies of Yamashita and Barka. In fact, '163 teaches cell medium that requires tri-iodothyronine or an ethanolamine compound. See col. 5, lines 25-60 and claims. These limitations are similar to the deficiencies identified in Yamashita. Therefore, even viewed as a whole, Yamashita, Barka, and '163 do not teach or suggest all the limitations of the current invention.

Because the cited references do not teach or suggest the claimed invention, reconsideration and withdrawal of the rejections of the claims are respectfully requested.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

It is acknowledged that the foregoing amendments are submitted after final rejection. However, because the amendments do not introduce new matter or raise new issues, and because the amendments either place the application in condition for allowance or at least in better condition for appeal, entry thereof by the Examiner is respectfully requested.

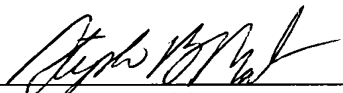
The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant(s) hereby petition(s) for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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